

What is claimed is:

- 5 1. A polypeptide having a sequence corresponding to the sequence of a portion of a chemokine receptor and capable of inhibiting the fusion of HIV-1 to CD4⁺ cells and thus of inhibiting HIV-1 infection of the cells.
- 10 2. A polypeptide having a sequence corresponding to the sequence of a portion of the chemokine receptor, CCR5 and capable of inhibiting the fusion of HIV-1 to CD4⁺ cells and thus of inhibiting HIV-1 infection of the cells.
- 15 3. The polypeptide of claim 2 comprising amino acids having a sequence of at least one extracellular domain of CCR5.
- 20 4. The polypeptide of claim 3 wherein the extracellular domain is the second extracellular loop.
- 25 5. A pharmaceutical composition comprising an amount of the polypeptide of claim 1 effective to inhibit the fusion of HIV-1 to CD4⁺ cells and a pharmaceutically acceptable carrier.
- 30 6. A polypeptide having a sequence corresponding to that of a portion of a HIV-1 envelope glycoprotein capable of specifically binding to the chemokine receptor CCR5.
- 35 7. The polypeptide of claim 6, wherein the glycoprotein is gp120.
8. A pharmaceutical composition comprising an effective amount of the polypeptide of claim 6 effective to inhibit the fusion of HIV-1 to CD4⁺ cells and a

pharmaceutically acceptable carrier.

5 9. An antibody or a portion of an antibody capable of binding to a chemokine receptor on a CD4⁺ cell and inhibiting HIV-1 infection of the cell.

10 10. A pharmaceutical composition comprising an amount of the antibody of claim 9 effective to inhibit HIV-1 infection of CD4⁺ cells and a pharmaceutically acceptable carrier.

15 11. A method of treating an HIV-1 infected subject which comprises administering to the subject the polypeptide of any of claims 1, 2, 3, 4, 6, or 7 in an amount effective to inhibit the fusion of HIV-1 to CD4⁺ cells of the subject and thus treat the subject.

20 12. A method of reducing the likelihood of a subject from becoming infected by HIV-1 which comprises administering to the subject the polypeptide of any of claims 1, 2, 3, 4, 6, or 7 in an amount effective to inhibit the fusion of HIV-1 to CD4⁺ cells of the subject and thus reduce the likelihood of HIV-1 infection.

25 13. A method for inhibiting HIV-1 infection of CD4⁺ cells which comprises contacting such CD4⁺ cells with a non-chemokine agent capable of binding to the chemokine receptor CCR5 in an amount and under conditions such that fusion of HIV-1 to the CD4⁺ cells is inhibited, thereby inhibiting HIV-1 infection of the cells.

30 14. The method of claim 13, wherein the non-chemokine agent is an oligopeptide.

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15. The method of claim 13, wherein the non-chemokine agent is a polypeptide.
- 5 16. The method of claim 13, wherein the non-chemokine agent is a nonpeptidyl agent.
- 10 17. A non-chemokine agent capable of binding to the chemokine receptor CCR5 and inhibiting the fusion of HIV-1 to CD4⁺ cells.
- 15 18. A pharmaceutical composition comprising an amount of the non-chemokine agent capable of binding to the chemokine receptor CCR5 and inhibiting the fusion of HIV-1 to CD4⁺ cells effective to inhibit HIV-1 infection of CD4⁺ cells and a pharmaceutically acceptable carrier.
- 20 19. A molecule capable of binding to the chemokine receptor CCR5 and inhibiting fusion of HIV-1 to CD4⁺ cells comprising a non-chemokine agent linked to a ligand capable of binding to a cell surface receptor of the CD4⁺ cells other than the chemokine receptor such that the binding of the non-chemokine agent to the chemokine receptor does not prevent the binding of the ligand to the other receptor.
- 25 20. The molecule of claim 18, wherein the cell surface receptor is CD4.
- 30 21. The molecule of claim 18, wherein the ligand comprises an antibody or a portion of an antibody.
- 35 22. A molecule capable of binding to the chemokine receptor CCR5 and inhibiting fusion of HIV-1 to CD4⁺ cells comprising a non-chemokine agent linked to a compound

capable of increasing the *in vivo* half-life of the non-chemokine agent.

23. The molecule of claim 21, wherein the compound is polyethylene glycol.

24. A pharmaceutical composition comprising an amount of the molecule of claim 19, 20, 21, 22 or 23 effective to inhibit fusion of HIV-1 to CD4⁺ cells and a pharmaceutically acceptable carrier.

25. A method for reducing the likelihood of HIV-1 infection in a subject comprising administering the pharmaceutical composition of claim 19, 20, 21, 22 or 23 to the subject.

26. A method for treating HIV-1 infection in a subject comprising administering the pharmaceutical composition of claim 19, 20, 21, 22 or 23 to the subject.

27. A method for determining whether a non-chemokine agent is capable of inhibiting the fusion of HIV-1 to a CD4⁺, CCR5⁺ cell which comprises:

(a) contacting the CD4⁺, CCR5⁺ cell, after it is labeled with a first dye, with a cell expressing an appropriate HIV-1 envelope glycoprotein on its surface, and labeled with a second dye, in the presence of an excess of the agent under conditions permitting fusion of the CD4⁺, CCR5⁺ cell to the cell expressing the HIV-1 envelope glycoprotein on its surface in the absence of an agent known to inhibit fusion of HIV-1 to CD4⁺, CCR5⁺ cells, the first and second dyes being selected so as to allow resonance energy transfer between the dyes;

- (b) exposing the product of step (a) to conditions which would result in resonance energy transfer if fusion has occurred; and
- (c) determining whether there is resonance energy transfer, the absence or reduction of transfer indicating that the agent is capable of inhibiting fusion of HIV-1 to CD4⁺ and CCR5⁺ cells.

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- 10 28. The method of claim 27, wherein the agent is an oligopeptide, a polypeptide or a nonpeptidyl agent.
- 29. The method of claim 27, wherein the CD4⁺ cell is a PM1 cell.
- 15 30. The method of claim 27, wherein the cell expressing the HIV-1 envelope glycoprotein is a HeLa cell expressing HIV-1_{JR-FL} gp120/gp41.
- 20 31. A transgenic nonhuman animal which comprises an isolated DNA molecule encoding the chemokine receptor CCR5.
- 25 32. The transgenic nonhuman animal of claim 31 further comprising an isolated DNA molecule encoding a sufficient portion of the CD4 molecule to permit binding the HIV-1 envelope glycoprotein.
- 30 33. A transgenic nonhuman animal which comprises an isolated DNA molecule encoding the chemokine receptor CCR5 and an isolated DNA molecule encoding fusin.
- 35 34. The transgenic nonhuman animal of claim 33 further comprising an isolated DNA molecule encoding a sufficient portion of the CD4 molecule to permit

binding the HIV-1 envelope glycoprotein.

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35. A transformed cell which comprises an isolated nucleic acid molecule encoding the chemokine receptor CCR5.
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36. An agent capable of inhibiting HIV-1 infection and capable of binding to a chemokine receptor without substantially affecting the said chemokine receptor's capability to bind to chemokines.
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37. The agent of claim 36, wherein the said chemokine receptor is CCR5.
38. The agent of claim 36, wherein after the binding of the agent to the said chemokine receptor, a two fold higher concentration of the chemokine is required to achieve the degree of binding observed if the chemokine receptor had not been bound to the agent.
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39. The agent of claim 36, wherein after the binding of the agent to the said chemokine receptor, a ten fold higher concentration of chemokine is required to achieve the degree of binding observed if the chemokine receptor had not been bound to the agent.
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40. The agent of claim 36, wherein the agent is an oligopeptide, a nonpeptidyl agent or a polypeptide.
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41. The agent of claim 40, wherein the polypeptide is an antibody or a portion of an antibody.
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42. A pharmaceutical composition comprising an amount of the agent of claim 37, 38, 39, 40 or 41 effective to inhibit fusion of HIV-1 infection and a pharmaceutically acceptable carrier.

43. A method for inhibiting HIV-1 infection of CD4⁺ cells which comprises contacting such CD4⁺ cells with an agent capable of inhibiting HIV-1 infection and capable of binding to a chemokine receptor without substantially affecting the said chemokine receptor's capability to bind to chemokines.
44. A molecule capable of binding to the chemokine receptor CCR5 and inhibiting fusion of HIV-1 to CD4⁺ cells comprising the agent of claim 36 linked to a compound capable of increasing the *in vivo* half-life of the non-chemokine agent.
45. The molecule of claim 44, wherein the compound is polyethylene glycol.
46. A pharmaceutical composition comprising an amount of the molecule of claim 44 or 45 effective to inhibit fusion of HIV-1 to CD4⁺ cells and a pharmaceutically acceptable carrier.
47. A method for reducing the likelihood of HIV-1 infection in a subject comprising administering the pharmaceutical composition of claim 42 or 46 to the subject.
48. A method for treating HIV-1 infection in a subject comprising administering the pharmaceutical composition of claim 42 or 46 to the subject.